I. AMENDMENTS

In the specification:

Please amend page 68, lines 7 to 15 to recite as follows:

Expression level of human thymidylate synthase transcripts in different cell lines were quantified by using RT-PCR. Oligonucleotide primers for amplification of the human thymidylate synthase and B-actin were designed as follows: Thymidylate synthase sense primer 5'-GGGCAGATCCAACACATCC-3' (SEQ ID No. 1) (corresponding to bases 208-226 of thymidylate synthase cDNA sequence, Genbank Accession No. X02308), antisense primer 5'-GGTCAACTCCCTGTCCTGAA-3' (SEQ ID No. 2) (corresponding to bases 564-583), β-actin sense primer 5'-GCCAACACAGTGCTGTCTG-3' (SEQ ID No. 3) (corresponding to bases 2643-2661 of β-actin gene sequence, Genbank accession no. M10277) and antisense primer 5'-CTCCTGCTTGCTGATCCAC-3' (SEQ ID No. 4) (corresponding to bases 2937-2955).

Please insert the paper copy of the Sequence Listing attached hereto to the specification.

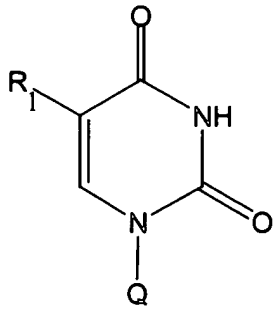
In the claims:

Cancel claim 1 without prejudice or disclaimer. Please amend claims 56 to 59, 61, 62, 64, 65, 67 to 70 and 86 to 88, as follows:

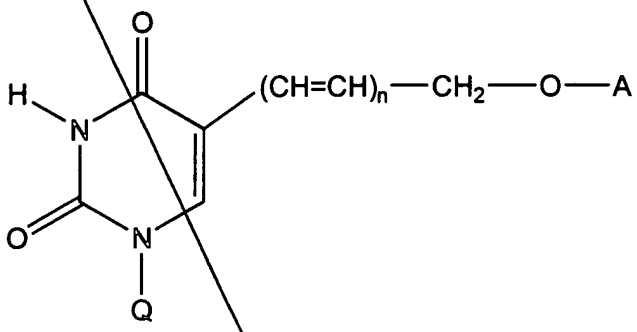
56. (Amended) A method for inhibiting the proliferation of a hyperproliferative cell, comprising contacting the cell with a phosphoryl or phosphoramidatyl prodrug that is selectively converted to a toxin in the cell by an endogenous, intracellular enzyme.

57. (Amended) A method for treating a pathology characterized by hyperproliferative cells in a subject comprising administering to the subject a phosphoryl or phosphoramidatyl prodrug that is converted to a toxin in a hyperproliferative cell by an intracellular enzyme that is endogenously overexpressed or over-accumulated in the cell.

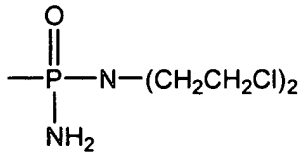
58. (Amended) A method for inhibiting the proliferation of a hyperproliferative cell comprising contacting the cell with an L- or D- isomer of the formula:



wherein R_1 is an electrophilic leaving group; or a compound of the formula:



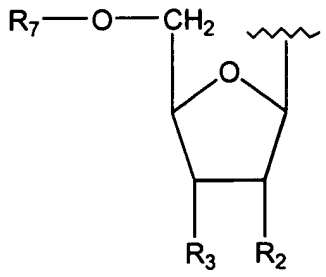
wherein n is an integer from 1 to 10; wherein A is a phosphoryl or phosphoramidatyl or a compound of the formula:



wherein Q is selected from the group consisting of a 5' substituted masked phosphoryl, a phosphoryl or phosphoramidatyl moiety selected from the group consisting of sugar; thio-sugar;

carbocyclic; acyclic analogs and derivatives of a sugar, a thio-sugar or a carbocyclic; derivatives, analogs and pharmaceutically acceptable salts thereof.

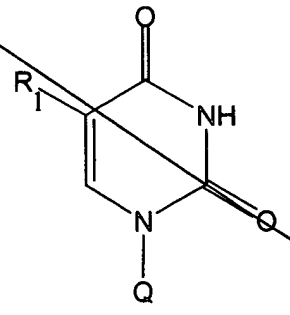
59. (Amended) The method of claim 58, wherein Q has the formula:



wherein R_7 is selected from the group consisting of masked phosphoryl moiety, phosphoramidatyl moiety, and wherein R_2 and R_3 are the same or different and are independently -H or -OH.

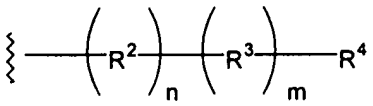
61. (Amended) The method of claim 58, wherein R_1 is of the formula $(-CH=CH)_n-R_4$, wherein n is an integer from 1 to 10, and R_4 is selected from the group consisting of H, a halogen, alkyl, alkenyl, alkynyl, hydroxyl -O-alkyl, -O-aryl, O-heteroaryl, -S-alkyl, -S-aryl, -S-heteroaryl, $-NH_2$, -NH-alkyl, $-N(alkyl)_2$, -NHCHO, -OCN, -SCN, $-N_3$, -NHOH, -NHO-alkyl, and $NHNH_2$.

62. (Amended) A compound of the formula:



wherein:

R^1 is of the formula:



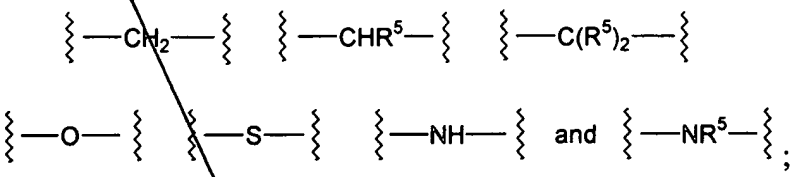
wherein n is from 1 to 10 and R^2 is selected from the group consisting of:

an unsaturated hydrocarbyl;

an aromatic hydrocarbyl; and,

a heteroaromatic;

R^3 is selected from the group consisting of:

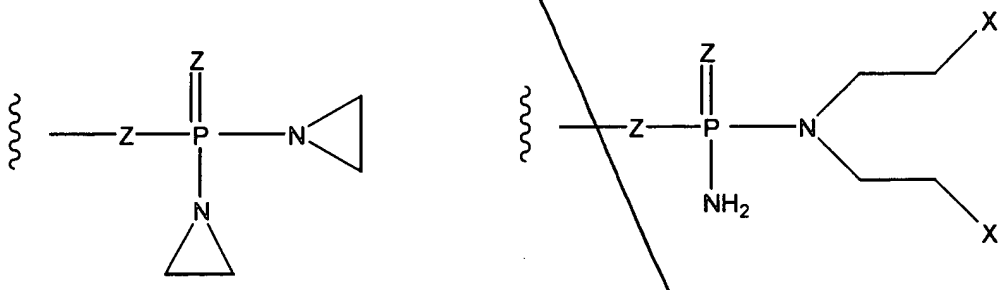


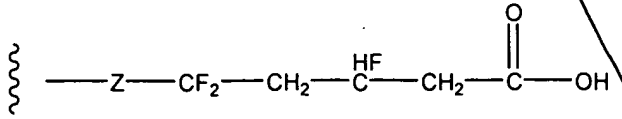
wherein R^5 may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;

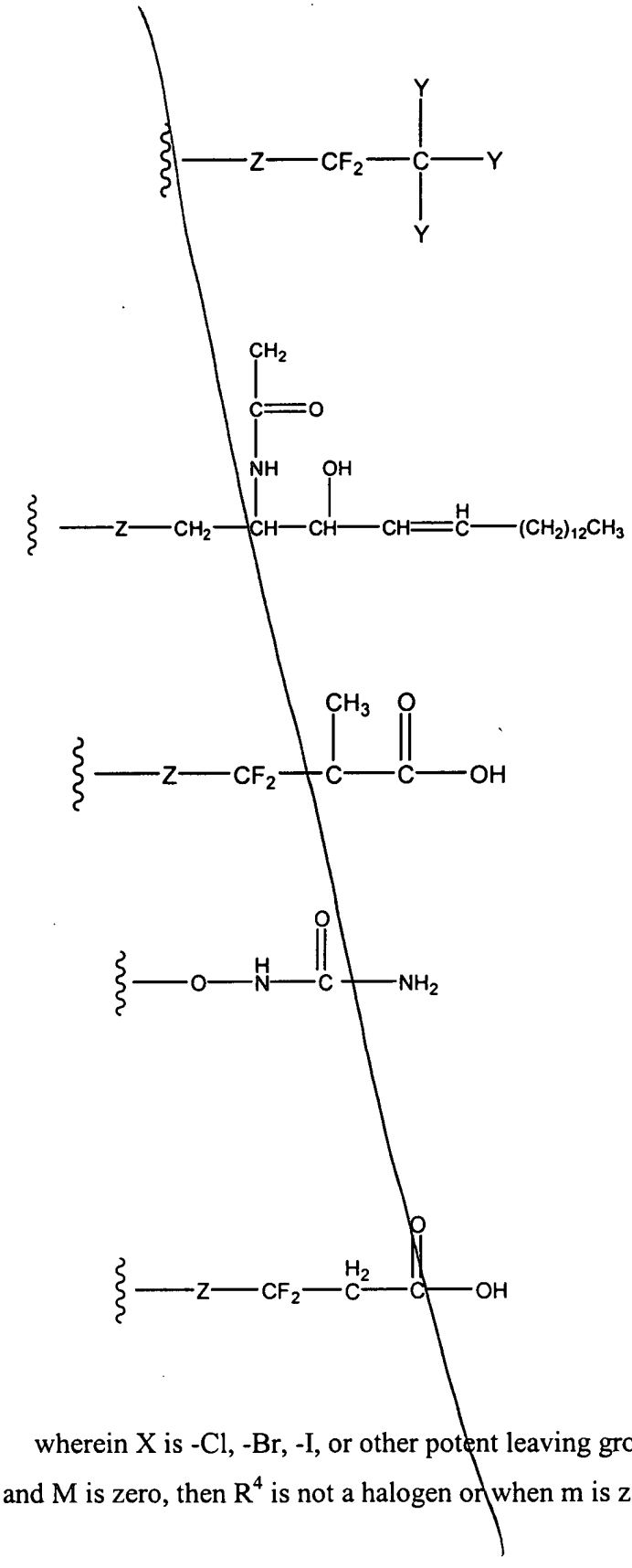
wherein n is an integer from 1 to 10;

wherein m is 0 or 1;

wherein R^4 is a toxophore selected from the group consisting of:







and

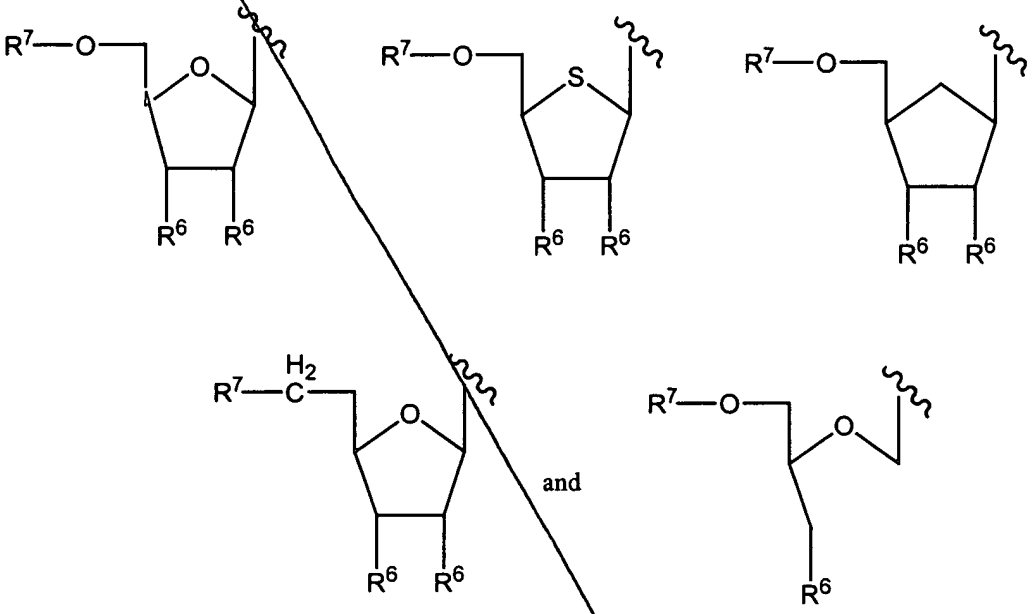
wherein X is -Cl, -Br, -I, or other potent leaving group, with the proviso that when R^7 is -H, and M is zero, then R^4 is not a halogen or when m is zero and n is zero, then

R^4 is not a halogen;

wherein Y is independently -H or -F;

wherein Z is independently -O- or -S-;

wherein Q is selected from the group consisting of:



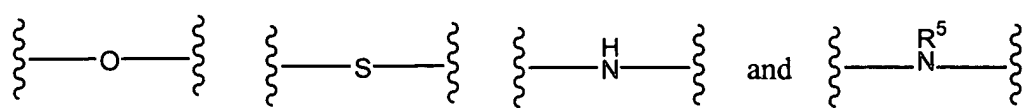
and

wherein R^6 is independently -H, -OH, $-OC(=O)CH_3$, or -O-Rg wherein Rg is a hydroxyl protecting group other than acetyl; and,

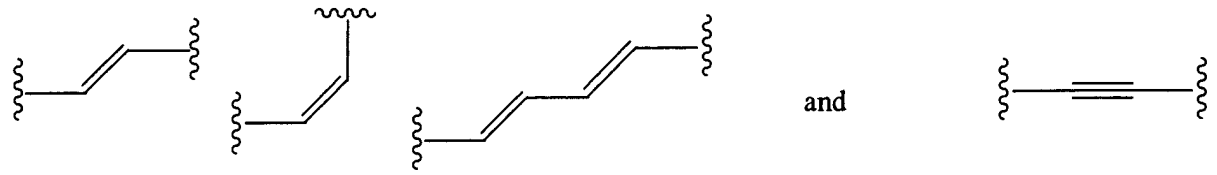
wherein R^7 is hydrogen, a masked phosphate group, or a phosphoramidatyl group;

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α-anomeric form, and β-anomeric form.

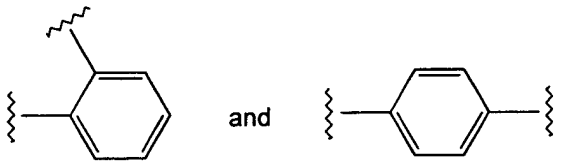
64. (Amended) A compound of claim 62, wherein R^3 is selected from the group consisting of:



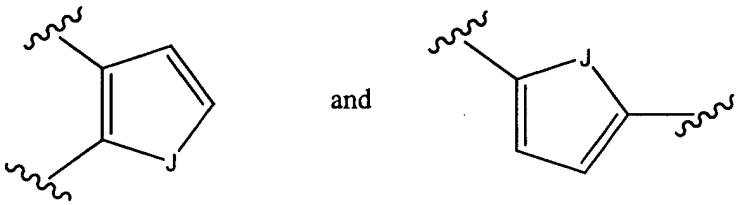
65. (Amended) A compound of claim 62, wherein R^2 is selected from the group consisting of:



67. (Amended) A compound of claim 62, wherein R^2 is selected from the group consisting of:

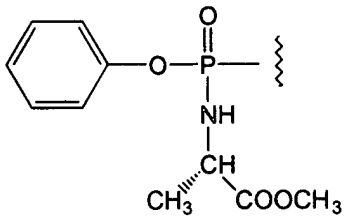


68. (Amended) A compound of claim 62, wherein R^2 is selected from the group consisting of:

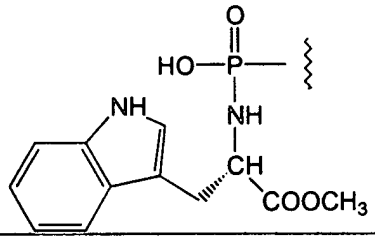


wherein J is -O-, -S-, -Se-, -NH-, or $-NR^{ALK}-$, wherein R^{ALK} is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms.

69. (Amended) A compound of claim 62, wherein R^7 is:



70. (Amended) A compound of claim 62, wherein R^7 is:



86. (Amended) A method of inhibiting the proliferation of a pathological cell that overexpresses an intracellular target enzyme, comprising:

(a) contacting the cell with a compound of claim 62; and

(b) allowing the cell to take-up and selectively convert the compound from an inactive state to an active toxic by-product by means of the intracellular target enzyme.

87. (Amended) A method of inhibiting the proliferation of a hyperproliferative cell that overexpresses intracellular enzymes and which contribute to drug resistance, comprising:

(a) contacting the cell with the compound of claim 62; and

(b) allowing the cell to take-up and selectively convert the compound from an inactive state to an active toxic byproduct by means of the enzyme.

88. (Amended) The method of claims 86 or 87, wherein the hyperproliferative cell is a cancer cell.